

Remarks:

In the Office Action dated December 3, 2003, the Office indicated claims 1-46 are pending and claims 5, 11, 17-28, and 30-46 are withdrawn from consideration, leaving claims 1-4, 6-10, 12-16, and 29 under consideration. In the Action, the Office rejected claim 13 under 35 U.S.C. § 102(b) or alternatively under 103(a), and claims 1-4, 6-10, 12-16, and 29 under 35 U.S.C. § 103(a).

Status of Withdrawn Claims

In response to the Restriction Requirement dated March 26, 2003, Applicant elected claims 1-18, 29-31, and 36. Further, in order to be responsive to the Office's election requirement, Applicant elected claims 1-4, 6-10, 12-16, and 29 as readable on the elected species. However, Applicant notes that claims 1-10, 12-16, and 29 are readable on the elected subgenus, and that claims 1-18, 29-31, and 36 are readable on the genus. Applicant respectfully reminds the Office of its duty under 35 U.S.C. § 121 and 37 C.F.R. § 1.141 to examine non-elected subject matter within the scope of claims 1-18, 29-31, and 36, upon a determination of allowable generic claims.

Rejections under 35 U.S.C. § 102

The Office rejects claim 13 under 35 U.S.C. § 102(b) or alternatively under 103(a) as unpatentable over Morrow (U.S. Patent No. 5,647,537). The Office asserts that Morrow expressly discloses singlet oxygen falling within the scope of the claim.

Applicants respectfully submit that the Office should consider the process elements of claim 13 in determining its patentability. Thus, while not agreeing with the Office's conclusion

regarding the patentability of claim 13, Applicant has canceled the claim in order to advance prosecution and remove issues for appeal.

Rejections under 35 U.S.C. § 103

The Office rejects claims 1-4, 6-10, 12-16, and 29 under 35 U.S.C. § 103(a) as being unpatentable over “the acknowledged prior art” in view of Beattie et al. (U.S. Patent No. 5,364,344).

The Patent Office Has Not Made a Prima Facie Case of Obviousness

Claim 1 is exemplary of the rejected claims. Claim 1 is directed to: “A method of treating a target site in or on a mammal, comprising: administering at least one source of peroxide and at least one source of hypochlorite anion to the target site to be treated, wherein the at least one source of peroxide and at least one source of hypochlorite are from separate sources, and allowing the peroxide and hypochlorite to react to produce singlet oxygen at the target site or during administration.”

As stated in the Manual of Patent Examining Procedure (M.P.E.P. § 2142), to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

There is No Suggestion or Motivation to Modify the Prior Art

The Office rejects the present claims over “acknowledged prior art” in view of Beattie et al. The Office appears to refer to two classes of alleged acknowledged prior art: 1) that relating to cell biology (e.g., Schraufstatter), which describes the natural cell-killing activity of neutrophils and their ability to produce, or cause the production of, hypochlorite and peroxide, and the cytotoxic mechanism of action of these oxidizing compounds; and 2) that relating to photodynamic therapy (e.g., McCaughan), which describes photodynamic therapy and/or the production of singlet oxygen by photooxidation of dye compounds. Applicant submits that the motivation to modify the prior art does not come from these references.

Cell Biology Art (e.g., Schraufstatter et al.)

The first class of art -- cell biology art -- simply describes current hypotheses on the functioning of eukaryotic cells. These cells are believed to produce, through complicated enzymatic processes, hydrogen peroxide, hypochlorite, and singlet oxygen, along with other potent oxidizing compounds, in phagocytosis activities. However, there is nothing in this class of teachings that would suggest the administration of at least one source of hypochlorite anion and at least one source of peroxide, so as to produce singlet oxygen at a target site. In fact, there is nothing in these teachings that would lead a person of skill in the art to any clinical application whatever. These teachings are directed to basic research and basic knowledge of cellular activities, and are simply inapplicable to the present invention.

Photodynamic Therapy Art (e.g., McCaughan et al.)

The next class of art is the photodynamic therapy art. Photodynamic therapy generally involves infusing a photoactive compound into a patient and allowing the compound to collect in

a tumor that is to be targeted. The photoactive compound in the tumor is then irradiated with light energy. Applicant respectfully submits that there is nothing in these teachings that would lead one of skill in the art to *a different* method for producing singlet oxygen at a target site. There is nothing in these teachings that would direct one of skill in the art to Applicant's invention.¹

Dual Lumen Catheter Art (e.g., Beattie et al.)

The Office cites to Beattie et al. for the teaching of a dual lumen catheter. Applicant submits that the teaching of Beattie et al. no more suggests the present invention than it does administering vinegar and baking soda for an effervescent effect. There is nothing in Beattie et al. that suggests any particular compounds or substances for administration. Beattie et al. simply provides a means for administering two solutions simultaneously, *if one wanted to do so*. But given the art, there is no reason that one would want to administer at least one source of peroxide and at least one source of hypochlorite.

Thus, in view of the art, there is simply no reason one would be motivated to arrive at the presently claimed invention. Indeed, as discussed in more detail below, one of skill in the art would actually be motivated to avoid the present invention.

There is No Reasonable Expectation of Success

The second primary element of a *prima facie* case of obviousness is the requirement for a reasonable expectation of success. On this point, the Office has also failed. The art does not

¹ It is worth noting that Dr. Christopher Foote, who is credited with the discovery of the reaction between peroxide and hypochlorite to produce singlet oxygen, continues his own research in the field of photodynamic therapy of cancer and novel photo-oxidizable dyes. If there were indeed motivation to move in the direction of the present invention, one would think that Dr. Foote would have proceeded to the present invention.

provide, and the Office has failed to show, a reasonable expectation of success if the art is modified as the Office suggests.

There is nothing in the art that suggests that at least one source of hypochlorite can be safely administered for a tumoricidal effect *in vivo*. There is nothing in the art that suggests that at least one source of peroxide can be safely administered for a tumoricidal effect *in vivo*. And there is nothing that suggests that these two reactants can be combined at a target site to achieve a tumoricidal effect. There is simply no *reasonable* basis to believe one could achieve the present invention.

The present invention involves administration of two components that are, and were, widely believed to be toxic to living cells. In the absence of Applicant's disclosure, one could not reasonably have believed that the two could be administered to achieve a therapeutic effect. It can only be concluded that the Office's rejection is based on hindsight reasoning -- applying Applicant's discoveries against him to defeat patentability. This approach is absolutely contrary to the Patent Office's rules for patent examination and the Federal Circuit has repeatedly warned against it.

The Prior Art Does Not Teach All the Claim Limitations

The last primary requirement of a *prima facie* case of obviousness is that the prior art reference (or references when combined) must teach or suggest all the claim limitations. This requirement also is not satisfied in this instance.

Applicant's claim requires *administration of at least one source of peroxide and at least one source of hypochlorite* to allow for the *generation of singlet oxygen* at the target site. The cited prior art fails to teach either the administration of hypochlorite or the administration of

peroxide or their combination to produce singlet oxygen at a target site. In the absence of these teachings, the present invention is not taught. In the absence of these teachings, the rejection is untenable.

The Office's Arguments and Applicant's Response Thereto

The Office states that the difference between the prior art and the claimed invention is that the prior art does not expressly disclose the combination of sodium hypochlorite and hydrogen peroxide to treat tumors. (Office Action, page 4, lines 3-5.) In response, Applicant submits that the cited prior art does not disclose, teach, or suggest, either expressly or impliedly, administration of at least one source hypochlorite and at least one source of peroxide, for treatment of tumors. The Office implies that the only difference between the cited art and the claimed invention is that the cited art does not teach administration of the combination, when in fact, the cited art does not teach administration of either one, singly or in combination.

The Office Action concludes with reference to *Ex Parte Rubin*, 128 U.S.P.Q. 440 (Bd. App. 1959), which is cited for the proposition that it is obvious to reverse the order of prior art process steps. Applicant respectfully submits that the cited prior art does not teach *any* step of Applicant's claimed invention. *In re Burhans*, 69 U.S.P.Q. 330 (C.C.P.A. 1946), is cited by the Office for the proposition that selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results. Applicant respectfully reiterates that the cited prior art does not teach *any* of Applicant's claimed steps. The Office refers to *In re Gibson*, 5 U.S.P.Q. 230 (C.C.P.A. 1930) for the proposition that selection of any order of mixing ingredients is prima facie obvious. Applicant again submits that the cited prior art does not teach administration of *any* of Applicant's elements.

In sum, the Office refers to art (e.g., Schraufstatter) that relates to the natural cell-killing activity of neutrophils and their ability to produce, or cause the production of, hypochlorite and peroxide, and the cytotoxic mechanism of action of these oxidizing compounds. The Office also refers to art (e.g., McCaughan) that discusses photodynamic therapy and the production of singlet oxygen by photooxidation of dye compounds. But neither of these two types of art teach or suggest the *administration* of at least one source of hypochlorite and at least one source of peroxide. And reference to Beattie et al. does nothing to remedy these deficiencies, as it simply teaches a dual lumen catheter, which might be used for co-administration of *anything*.

The Office attributes to the art teachings that it simply does not provide. The best example of this is at page 4, lines 5-7, of the Action, where the Office sums up its conclusions regarding the art: “[T]he prior art amply suggests the same as it is known in the art that hypochlorites and peroxides are effective in treating tumor cells and that they also react to form singlet oxygen which is also effective against cancer and tumor cells.” With respect, Applicant submits that the art does not teach *treating* tumor cells with either peroxide or hypochlorite, and without more, does not teach the combination for production of singlet oxygen.

Additional Arguments in Favor of Nonobviousness

At the time this application was filed, it was widely recognized and accepted in the medical profession that peroxide and hypochlorite were toxic and should not be administered. Attached hereto is a printout from the American Cancer Society website that include statements regarding the use of hydrogen peroxide. The American Cancer Society’s position on hydrogen peroxide, which it recommends to all physicians and patients, was stated best when the Society said: “Although hydrogen peroxide is well known for its antiseptic properties, there is no evidence that it has value as a treatment for cancer or other diseases.”

As the Federal Circuit has repeatedly recognized, proceeding contrary to the accepted wisdom in the art represents “strong evidence of unobviousness.” *In re Hedges*, 783 F.2d at 1041, 228 U.S.P.Q. at 687; *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d at 1552, 220 U.S.P.Q. at 312 (prior art teaching that conventional polypropylene should have reduced crystallinity before stretching and should undergo slow stretching, led away from claimed process of producing porous article by expanding highly crystalline PTFE by rapid stretching); accord *In re Fine*, 837 F.2d at 1074, 5 U.S.P.Q. at 1599. And where a reference warns against rather than teaches an invention, one of skill in the art cannot be expected to combine it with another teaching. *Id.*

Applicant respectfully submits that the art, as represented in the cited statements above, clearly suggests that one *not* administer peroxide for treatment of cancer. This is strong evidence of the nonobviousness of the present invention, which requires, among other things, administration of at least one source of peroxide to a target site.

Statements regarding hypochlorite use are best summarized in the Material Safety Data Sheet for sodium hypochlorite, from the Clorox Company (“Health Hazard Data” section), a copy of which is provided as an attachment. Based on the warnings in this MSDS, hypochlorite is clearly regarded as a toxic substance. Applicant respectfully submits that one of skill in the art would not have administered at least one source of hypochlorite for treatment of cancer, given that the compound was known to be so toxic.

Thus, the art clearly establishes that peroxide and hypochlorite are toxic and potentially dangerous, and the American Cancer Society, while recognizing its antiseptic qualities, actually advises *against* the administration of peroxide in treating cancer or any other disease. And Applicant submits that the absence of a similar caution against the use of hypochlorite may be

telling in that no one has ever even advocated its administration, so a warning is unnecessary. It is respectfully submitted that the prior art clearly teaches away from the presently claimed invention.

Conclusion

Applicant respectfully requests that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 1-4, 6-10, 12-16, and 29 in condition for allowance. Applicant submits that the proposed cancellation of claim 13 does not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Furthermore, Applicant respectfully points out that the final action by the Examiner presented some new arguments as to the application of art against Applicant's invention. Applicant respectfully submits that the entering of the Amendment would allow Applicant to reply to the final rejections and place the application in condition for allowance.

Finally, Applicant submits that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicant submits that this claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicant therefore requests the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account number 03-0172.



Respectfully submitted,

Date: January 28, 2003

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Making Treatment Decisions

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Hydrogen Peroxide Therapy

Other common name(s): Hydrogen Peroxide

Scientific/medical name(s): H₂ O₂

Description

Hydrogen peroxide is a clear, odorless oxygen solution that is widely available for use in cleaning and disinfecting wounds. In high concentrations (eg, 35%), hydrogen peroxide is used by alternative practitioners as a treatment for cancer and other diseases.

Overview

Although hydrogen peroxide is well known for its antiseptic properties, there is no evidence that it has value as a treatment for cancer or other diseases. It can be toxic at concentrations above 10%.

How is it promoted for use?

Proponents claim that hydrogen peroxide therapy can be used to oxidize toxins, kill bacteria and viruses, and stimulate the immune system. It is promoted for everything from cleansing the digestive tract to curing cancer and other diseases such as arthritis. Some people advocate cleaning foods with it prior to eating.

Supporters of hydrogen peroxide therapy believe that cancer cells grow rapidly if they are deprived of oxygen. They claim that hydrogen peroxide can cure cancer by bombarding cancer cells with more oxygen than they can handle (see Oxygen Therapy).

What does it involve?

Hydrogen peroxide is used internally or injected. Some practitioners promote it for use rectally, vaginally, as a nasal spray, and as eardrops. It is often used to soak affected parts of the body. The stronger solution recommended by alternative medicine practitioners (about 35%) are sold in some health food stores.

Because of its antiseptic and whitening properties, hydrogen peroxide is found in some toothpastes and mouthwashes, usually at a 3% (or less) solution. In stronger solutions of about 10%, it is used as hair bleach, and in industry to bleach paper and cloth, to manufacture other chemicals, and as an ingredient in some rocket fuels.

What is the history behind it?

One of the earliest accounts of the scientific study of hydrogen peroxide was a short article by I.N. Love, MD, in 1888 in the Journal of the

American Medical Association. Dr. Love reported that the hydrogen peroxide was useful in treating diseases such as scarlet fever, diphtheria, cancer of the uterus, and pneumonia. In 1920, hydrogen peroxide injections were used to treat patients during an epidemic of viral pneumonia.

Many promoters base their claims on the ideas of Otto Warburg, a Nobel Prize winner in the 1930s. His theory was that cancer cells grow better under conditions where there are lower levels of oxygen. Contemporary use of hydrogen peroxide can be traced to Father Richard Wilhelm, a retired high school teacher and former Army chaplain. He claimed to have discovered the healing potential of hydrogen peroxide through acquaintance with a physician who headed the Mayo Clinic's division of experimental bacteriology, Edward Carl Rosenow, MD.

What is the evidence?

Medical researchers have studied hydrogen peroxide for over a century to determine if it can cure various diseases. In the 1940s, hydrogen peroxide was tested on animals to see if it could treat carbon monoxide poisoning, hemorrhage, and toxic reactions of exposure to certain chemicals. During the next three decades, many researchers studied the effects of hydrogen peroxide on tumors in laboratory animals. When used alone, hydrogen peroxide was not effective.

Some have investigated it as an addition to radiation therapy. Although some patients appeared to benefit, many did not. Attempts to treat patients with hydrogen peroxide injections directly into solid tumors or into the blood system have generally been ineffective. There is currently no scientific evidence that hydrogen peroxide therapy is effective for treating any of the conditions that have been claimed.

Are there any possible problems or complications?

Hydrogen peroxide can be harmful if swallowed. Drinking the concentrated solutions sold in some health food stores (35%) can cause vomiting, severe burns of the throat and stomach, and even death. Direct skin contact or breathing the vapors of hydrogen peroxide can also be harmful.

Hydrogen peroxide injections can have dangerous side effects. High blood levels of hydrogen peroxide create oxygen bubbles that can block blood flow and cause gangrene and death. Acute hemolytic crisis (destruction of blood cells) has also been reported following intravenous injection of hydrogen peroxide. Women who are pregnant or breast-feeding should not use this method.

References

American Cancer Society. Questionable methods of cancer management: hydrogen peroxide and other 'hyperoxygenation' therapies. CA Cancer J Clin. 1993;43:47-56.

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Green S. Hyperoxygenation Therapy. Healthcare Reality Check Web site. Available at: <http://www.hcrc.org/faqs/hyperox.html>. Accessed October 19, 1999.

Hirschtick RE, Dyrda SE, Peterson LC. Death from an unconventional therapy for AIDS. *Ann Intern Med.* 1994;120:694.

Murphy GP, Morris LB, Lange D. *Informed Decisions: The Complete Book of Cancer Diagnosis, Treatment, and Recovery.* New York, NY: Viking; 1997.

Sherman SJ, Boyer LV, Sibley WA. Cerebral infarction immediately after ingestion of hydrogen peroxide solution. *Stroke.* 1994;25:1065-1067.

US Congress, Office of Technology Assessment. *Unconventional Cancer Treatments.* Washington, DC: US Government Printing Office, 1990. Publication OTA-H-405.

Note: This information was reprinted from the American Cancer Society's *Guide to Complementary and Alternative Methods.* Copyright(c)2000, American Cancer Society. This information may not cover all possible claims, uses, actions, precautions, side effects or interactions, is not intended as medical advice, and should not be relied upon as a substitute for consultation with your doctor who is familiar with your medical needs.



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Material Safety Data Sheet

CLOROX-HMIS	
HEALTH	2*
FLAMMABILITY	0
REACTIVITY	1
Personal Protection	B

I Chemical Identification								
NAME: LEMON FRESH CLOROX		CAS no. N/A						
DESCRIPTION: FRAGRANCED BLEACH		RTECS no. N/A						
Other Designations		Manufacturer						
Sodium hypochlorite Liquid chlorine bleach EPA Reg. No. 5813-20		The Clorox Company 1221 Broadway Oakland, CA 94612						
Emergency Procedures								
Notify your Supervisor Call your local poison control Center or Rocky Mountain Poison Center (303) 573-1014								
II Health Hazard Data		III Hazardous Ingredients						
<p>*Causes severe but temporary eye injury. May irritate skin. May cause nausea and vomiting if ingested. Exposure to vapor or mist may irritate nose, throat and lungs. The following medical conditions may be aggravated by exposure to high concentrations of vapor or mist: heart conditions or chronic respiratory problems such as asthma, chronic bronchitis or obstructive lung disease. Under normal consumer use conditions the likelihood of any adverse health effects are low. FIRST AID: EYE CONTACT: Immediately flush eyes with plenty of water. If irritation persists, see a doctor. SKIN CONTACT: Remove contaminated clothing. Wash area with water. INGESTION: Drink a glassful of water and call a physician. INHALATION: If breathing problems develop, remove to fresh air.</p>		<table><thead><tr><th>Ingredients</th><th>Concentration</th><th>Worker Exposure Limit</th></tr></thead><tbody><tr><td>Sodium hypochlorite CAS# 7681-52-9</td><td>5.25%</td><td>not established</td></tr></tbody></table> <p>None of the ingredients in this product are on the IARC, OSHA or NTP carcinogen lists. Occasional clinical reports suggest a low potential for sensitization upon exaggerated exposure to sodium hypochlorite if skin damage (eg. irritation) occurs during exposure. Routine clinical tests conducted on intact skin with Lemon Fresh Scent found no sensitization in the test subjects.</p>	Ingredients	Concentration	Worker Exposure Limit	Sodium hypochlorite CAS# 7681-52-9	5.25%	not established
Ingredients	Concentration	Worker Exposure Limit						
Sodium hypochlorite CAS# 7681-52-9	5.25%	not established						
IV Special Protection Information		V Special Precautions						
<p>Hygienic Practices: Wear safety glasses and gloves.</p> <p>Engineering Controls: Use general ventilation to minimize exposure to vapor or mist</p> <p>Work Practices: Avoid eye and skin contact and inhalation of vapor or mist</p>		<p>Keep out of reach of children. Do not get in eyes or on skin. Wash thoroughly with soap and water after handling. Do not mix with other household chemicals such as toilet bowl cleaners, rust removers, vinegar, acid or ammonia containing products. Store in a cool, dry place. Do not reuse empty container; rinse container and put in trash container. Do not use for food or water treatment.</p> <p>This product is not registered with the EPA as a disinfectant.</p>						
VI Spill or Leak Procedures		VII Reactivity Data						
<p>Small quantities of less than 5 gallons may be flushed down drain. For larger quantities wipe up with an absorbent material or mop and dispose of in accordance with local, state and federal regulations. Dilute with water to minimize oxidizing effect on spilled surface.</p>		<p>Stable under normal use and storage conditions. Strong oxidizing agent. Reacts with other household chemicals such as toilet bowl cleaners, rust removers, vinegar, acids or ammonia containing products to produce hazardous gases, such as chlorine and other chlorinated species. Prolonged contact with metal may cause pitting or discoloration.</p>						
VIII Fire and Explosion Data		IX Physical Data						
<p>Not flammable or explosive. In a fire, cool containers to prevent rupture and release of sodium chlorate.</p>		<p>Boiling point-----212°F/100°C (decomposes) Specific Gravity (H₂O=1)-----1.085 Solubility in Water-----complete pH-----12.5</p>						